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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/784,908	02/23/2004	Henry R. Costantino	1733.1064-004	6133

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EXAMINER	
NAFF, DAVID M	
ART UNIT	PAPER NUMBER
1657	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/784,908	COSTANTINO ET AL	
	Examiner	Art Unit	
	David M. Naff	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2006*.

2a)☒ This action is FINAL. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment of 10/16/06 responding to an office action of 4/11/06 amended claim 1.

Claims examined on the merits are 1-22, which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Adequate support is not found in the specification for "retention or growth surface" in line 5 of claim 1. While the specification (page 6, lines 8 and 9) discloses that the microparticles contribute to the retention of the cells at the treatment site, this does not disclose that the microparticles provide a retention surface for cells. The microparticles are disclosed as providing a surface for

growth of cells and not a surface for retention of cells. The specification does not disclose how the microparticles provide retention of the cells. To be consistent with the specification, claim 1 should be amended in line 5 by canceling "a" before "retention", after "retention" inserting --- of the cells at the treatment site ---, and before "growth" inserting --- a ---.

Claim Rejections - 35 USC § 102

Claims 1-5 and 13-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Mooney et al (6,281,015 B1).

The claims are drawn to a method of administering cells to a patient comprising injecting into a treatment site of a patient without open surgery to expose the treatment site a composition containing biodegradable, polymer microparticles and cells in an amount sufficient to provide a therapeutic effect in the patient. The therapeutic effect can be generation of new tissue.

Mooney et al disclose administering to a patient microspheres containing bioactive factors such as growth factors (TGFß), angiogenic factors or hormones such as insulin, glucagons and estrogen (col 8, lines 31-42) and cells that form cartilage (chondrocytes) (col 9, line 19). The cells and microspheres are suspended in or attached to a polymer matrix (paragraph bridging cols 8 and 9). The microspheres and cells can be suspended in a polymer solution and injected into a patient prior to hardening of the suspension (col 9, lines 26-38, col 12, lines 1-9, and col 18, claims 3 and 4). The concentration of cells can be between 1 and 50 million cells/ml (col 12, line 8) such

as $50x10^6$ cells/ml (col 16, line 51) or $5x10^7$ cells/ml (col 17, line 21).

Mooney et al disclose a method that is the same as presently claimed. The claims do not exclude injecting a polymer solution containing microspheres and cells as disclosed by Mooney et al. A morphogenic protein as in claims 20 and 21 is alternative to a growth factor and is not required by the claims when a growth factor is selected as the alternative.

Response to Arguments

The amendment urges that Mooney et al administer microparticles in a fibrous structure or a polymer solution. However, the present claims do not exclude the microparticles being in polymer solution when injected and the polymer solution forming a matrix after injection. Since both the cells and microparticles are in the polymer solution of Mooney et al before injection and after injection during hardening of the polymer solution, the cells are in contact with the microparticles before and after injection, and will be in contact with the microparticles in the matrix. Therefore, it would have been obvious that the surface of the microspheres of Mooney et al will provide a retention or growth surface for cells in the matrix. The microsparticles and cells of Mooney et al being in a matrix *in vivo* will not prevent the microparticles functioning as claimed as a retention or growth surface for the cells since the cells are in contact the microparticles inside the matrix.

The amendment urges that delivery of a polymer solution to a particular area is difficult. However, since Mooney et al inject a polymer solution and the claims do not exclude the cells and microparticles being in a polymer solution when injected at a treatment site, injection of a polymer solution is not sufficiently difficult to lead one away from injecting a polymer solution containing the microparticles and cells.

Claim Rejections - 35 USC § 102

Claims 1-5 and 13-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Mooney et al (WO 96/18411).

The claimed invention is described above.

The disclosure of Mooney et al (WO 96/18411) is the same as the disclosure of Mooney et al (6,281,015 B1).

Mooney et al (WO 96/18411) disclose the presently claimed method.

Response to Arguments

The response to arguments set forth above also applies to this rejection since the same arguments in the amendment apply to both the above rejection and this rejection.

Claim Rejections - 35 USC § 103

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mooney et al (WO 96/18411) or (6,281,015 B1) in view of Purchio et al (5,902,741).

The claim requires the treatment site to be the articular space of a joint.

Mooney et al (WO 96/18411) and (6,281,015 B1) are described above.

Purchio et al disclose *in vitro* culturing of cells on a three-dimensional framework to produce cartilage tissue for use in repairing articular cartilage of a joint (col 2, line 30 to col 3, line 21, col 6, lines 8-31, and col 15, lines 40-51).

It would have been obvious to produce articular cartilage as the cartilage produced by Mooney et al (WO 96/18411) or (6,281,015 B1) to obtain cartilage for use in repairing articular cartilage of a joint as suggested by Purchio et al.

Response to Arguments

The above response to the argument, urging that the microparticles of Mooney et al do not provide a retention and growth surface for cells, also applies to this rejection. While Purchio et al is not using microparticles, the use of microparticles to provide a retention or growth surface for cells is rendered obvious by Mooney et al. The references are applied together, and the invention becomes obvious when the references are considered in combination rather than each alone. Purchio et al is relied on to suggest injecting the cells of Mooney et al into the articular space of a joint when this is a site cartilage production is desired.

Claim Rejections - 35 USC § 103

Claims 7-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mooney et al (WO 96/18411) or (6,281,015 B1) in view of Holland et al (5,550,050).

The claims require the secretion of a biologically active secretory molecule to provide the therapeutic effect.

Mooney et al (WO 96/18411) and (6,281,015 B1) are described above.

Holland et al disclose implanting in a host encapsulated secretory cells that release therapeutic substances (col 3, lines 19-25, and col 12, lines 15-20). The cells can be PC12 cells (col 6, line 33), pancreatic islet cells (col 9, lines 5-10) or adrenal chromaffin cells (col 15, lines 15-20). The therapeutic substance can be insulin (col 9, lines 39 and 49, and col 10, line 18) or dopamine (col 10, lines 28 and 31).

It would have been obvious to include secretory cells as cells implanted by Mooney et al (WO 96/18411) or (6,281,015 B1) to obtain the function of the cells to produce a therapeutic substance as suggested by Holland et al. Bioactive substances disclosed by Mooney et al (WO 96/18411) or (6,281,015 B1) can be the same as therapeutic substances disclosed by Holland et al, and producing these substances or other therapeutic substances with secretory cells would have been obvious from the use of secretory cells taught by Holland et al.

Response to Arguments

The above response to the argument, urging that the microparticles of Mooney et al do not provide a retention and growth surface for cells, also applies to this rejection. While Holland et al is not using microparticles, the use of microparticles to provide a retention or growth surface for cells is rendered obvious by Mooney et

al. The references are applied together, and the invention becomes obvious when the references are considered in combination rather than each alone. Holland et al is relied on to suggest including secretory cells with the cells of Mooney et al to produce a biologically active secretory molecule when the function of such a molecule is needed.

Claim Rejections - 35 USC § 103

Claims 1-5 and 13-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mooney et al (WO 96/18411) or (6,281,015 B1) in view of Armstrong (5,830,507) and Dimoudis et al (5,980,888).

The invention and Mooney et al (WO 96/18411) and (6,281,015 B1) are described above.

Armstrong discloses forming skin replacement by treatment of a skin injury with a slurry of microspheres coated with cells.

Dimoudis et al disclose attaching keratinocytes to microcarriers to form a material for treatment of skin wounds.

It would have been obvious to omit the polymer matrix or polymer solution of Mooney et al (WO 96/18411) or (6,281,015 B1) and allow the cells to grow on the microspheres and produce tissue as suggested by Armstrong and Dimoudis et al using cells attached to microcarriers to form new skin tissue. The conditions of dependent claims are disclosed by (WO 96/18411) or (6,281,015 B1), or would have been obvious from conditions disclosed by the references.

Response to Arguments

Contrary to the argument in the amendment, this rejection is not based on the microparticles of Mooney et al not providing a surface

for retention and growth of cells. The rejection is based on Armstrong and Dimoudis et al suggesting that the microparticles of Mooney et al can be injected without the microparticles and cells being in a polymer solution that forms a matrix. The above response to the argument, urging that the microparticles of Mooney et al do not provide a retention and growth surface for cells, also applies to this rejection. While Armstrong and Dimoudis et al treat skin wounds and do not inject microparticles and cells, it would have been obvious when Mooney et al is considered that cells and microparticles can be injected to a site where new tissue is desired. The references are applied together, and the invention becomes obvious when the references are considered in combination rather than each alone. There is seen nothing sufficient to lead one to believe microspheres coated with cells as disclosed by Armstrong and Dimoudis et al cannot be injected at a site as disclosed by Mooney et al for tissue repair when the cells are cells specific for repairing the tissue desired to be repaired.

Claim Rejections - 35 USC § 103

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-5 and 13-22 above, and further in view of Purchio et al.

The claimed invention and the references are described above.

When modifying Mooney et al (WO 96/18411) or (6,281,015 B1) by omitting the polymer matrix or polymer solution as set forth above, it would have been obvious to produce articular cartilage as the

cartilage produced by Mooney et al (WO 96/18411) or (6,281,015 B1) to obtain cartilage for use in repairing articular cartilage of a joint as suggested by Purchio et al.

Response to Arguments

Arguments traversing this rejection are unpersuasive for the type of reasons set forth above when responding to arguments traversing the rejection of claim 6.

Claim Rejections - 35 USC § 103

Claims 7-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-5 and 13-22 above, and further in view of Holland et al.

The claimed invention and the references are described above.

When modifying Mooney et al (WO 96/18411) or (6,281,015 B1) by omitting the polymer matrix or polymer solution as set forth above, it would have been obvious to include secretory cells as cells implanted by Mooney et al (WO 96/18411) or (6,281,015 B1) to obtain the function of the cells to produce a therapeutic substance as suggested by Holland et al. Bioactive substances disclosed by Mooney et al (WO 96/18411) or (6,281,015 B1) can be the same as therapeutic substances disclosed by Holland et al, and producing these substances or other therapeutic substances with secretory cells would have been obvious from the use of secretory cells taught by Holland et al.

Vogel et al (6,660,301 B1) is made of record to further disclose injecting microparticles and cells.

Response to Arguments

The type of response set forth above in regard to arguments traversing the rejection of claims 7-12 also applies to this rejection of the claims.

Double Patenting

Claims 1-5 and 13-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,719,970 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the presently claimed method of injecting cells and microparticles would have been obvious from the method claimed by the patent of generating cartilage by injecting chondrocytes and microparticles.

Double Patenting

Claim 6 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,719,970 B1 in view of Purchio et al.

It would have been obvious to produce articular cartilage as the cartilage produced by method of the patent claims to obtain cartilage for use in repairing articular cartilage of a joint as suggested by Purchio et al.

Double Patenting

Claims 7-12 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,719,970 B1 in view of Holland et al.

It would have been obvious to include secretory cells as cells implanted by the method of the patent claims to obtain the function of the cells to produce a therapeutic substance as suggested by Holland et al. Biologically active agents required by certain claims of the patent can be the same as therapeutic substances disclosed by Holland et al, and producing these agents with secretory cells would have been obvious from the use of secretory cells taught by Holland et al.

Response to Arguments

In responding to the above double patenting rejections, the amendment indicates that terminal disclaimers will be considered upon an indication of otherwise allowable subject matter.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

David M. Naff
Primary Examiner
Art Unit 1657

DMN
1/16/07